

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference F04-022PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/JP2004/019454	International filing date (<i>day/month/year</i>) 17 December 2004 (17.12.2004)	Priority date (<i>day/month/year</i>) 22 December 2003 (22.12.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant ASTELLAS PHARMA INC.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland		Date of issuance of this report 26 June 2006 (26.06.2006)
Facsimile No. +41 22 338 82 70		Authorized officer Masashi Honda
Form PCT/IB/373 (January 2004)		e-mail: pt08@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 17 MAR 2006

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To:

OMM

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/JP2004/019454

International filing date (day/month/year)
17.12.2004

Priority date (day/month/year)
22.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07D307B5, C07D209/42, C07D215/48, C07D471/04

Applicant
ASTELLAS PHARMA INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2004/019454

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2004/019454

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2004/019454

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	2-19
Inventive step (IS)	Yes: Claims	
	No: Claims	2-19
Industrial applicability (IA)	Yes: Claims	2-19
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/JP2004/019454

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims 1 as well as 2 may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). Claim 1 could not be searched. For these reasons, the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 2-19.

The search of claims 2 to 19 was further restricted to:
compounds of general formula (Ia) and (Ib) wherein R^2 , R^7 as well as n have the meaning given in claim 3 and valid for compounds of formula (Ib).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: EP-A-1 389 460 (KUREHA CHEMICAL INDUSTRY CO., LTD) 18 February 2004 (2004-02-18)
- D2: WO 02/44175 A2 (CIS BIO INTERNATIONAL, FR.) 6 June 2002 (2002-06-06)
- D3: EP-A-1 273 571 (KUREHA CHEMICAL INDUSTRY CO., LTD) 8 January 2003 (2003-01-08)
- D4: EP-A2-0 498 941 (BOC HEALTH CARE, INC., USA) 19 August 1992 (1992-08-19)
- D5: DE 35 44 338 A1 (HOECHST A.-G. , FED. REP. GER.) 19 June 1987 (1987-06-19)
- D6: WO 00/16760 A (FUJISAWA PHARMACEUTICAL CO., LTD; KOHNO, YUTAKA; TENDA, YOSHIYUKI; NAK) 30 March 2000 (2000-03-30)
- D7: MAO G-F ET AL: "Prostaglandin E2 Both Stimulates and Inhibits Adenyl Cyclase on Platelets: Comparison of Effects on Cloned EP4 and EP3 Prostaglandin Receptor Subtypes" PROSTAGLANDINS, BUTTERWORTH, STONEHAM, MA, US, vol. 52, no. 3, September 1996 (1996-09), pages 175-

185, XP004070268 ISSN: 0090-6980

D8: US-B1-6 437 146 (HATTORI KOUJI ET AL) 20 August 2002 (2002-08-20)

Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 2-19 is not new in the sense of Article 33(2) PCT.

Applicant's attention is drawn to each single compound, example or table cited in the search report and regarding documents D1 to D5. By restoring the novelty of the subject-matter claimed, the applicant should clearly indicate the novelty rendering feature(s) of the whole invention (compounds of both formula (Ia) as well as (Ib).

Inventive step

Until such a time as claims are available which satisfy the conditions of novelty a final decision on inventive step cannot be made.

However the Examiner wishes to stress some relevant points already at this stage of the procedure:

The problem underlying the present application is seen in the provision of further derivatives which are useful for treating or preventing PGE₂ mediated diseases.

PGE₂ antagonists are known from i.a. D6 (the only document cited which defines the general state of the art) and relates to oxazole compounds of general formula (I) which are structurally quite remote.

D7 relates to the examination of the effects of prostaglandin E₂ (PGE₂) on platelet cyclic AMP formation also compared with effects on cloned prostaglandin receptors.

The present inventors found that the compounds having an ornithine derivative skeleton bind preferentially to PGE₂ receptor and are, thus, useful in the treatment and/or prevention of PGE₂ mediated diseases as listed on page 3.

In the absence of any relevant prior art, the significant difference illustrates the non obviousness of the claimed compounds, and can thus, indeed form an argument in support of the presence of an inventive step. However, the technical problem underlying the invention should be also solved and evidences in support for the claimed solution are, presently, only given in terms of binding assay for one single compound. Further evidence is needed.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/JP2004/019454